

Amendments to the specification:

Insert the following paragraph before the first paragraph of the specification:

This application is a division of, and claims priority to, application Serial No. 09/385,442, filed August 30, 1999, now U.S. Patent No. 6,200,954 B1. Serial No. 09/385,442 claimed priority to provisional application Serial No. 60/099,313, filed on September 4, 1998.

Amend the paragraph starting in line 16 on page 4 as indicated:

Some preferred peptides of the invention are named Angio-1, Angio-2, Angio-3, Angio-4 and Angio-5 (~~SEQ. ID. NOS. 1-3, 11, and 12~~ SEQ ID NOS: 1-3, 11, and 12) according to the plasminogen kringle domains they are derived from. Other preferred peptides are shown in Table 1 (~~SEQ ID NOS. 29-50~~ SEQ ID NOS: 29-50).

Amend the paragraph starting in line 11 on page 6 as indicated:

Angiostatin-derived peptides of the present invention represent a portion of a kringle domain of plasminogen. The effective portion of a kringle domain is generally residues 30 to 38 or 39 of a kringle domain, numbered as in reference 13. However, it is acceptable to add additional amino acids to this generally effective core peptide. Thus, peptides representing residues 27 to 40 or 41 of a kringle domain would be expected to be effective. Preferred peptides of the invention are derived from human or mouse plasminogen. The exemplified peptides of ~~SEQ. ID. NOS.: 1-3, 11 and 12~~ SEQ ID NOS: 1-3, 11, and 12 represent residues 29-38 or 29-39 of human plasminogen kringle domains (13).

Amend the paragraph starting in line 30 on page 6 as indicated:

The peptides also preferably contain a pair of proline residues. Each proline residue of the pair is preferably the residue penultimate to a terminus of a peptide, but either or both of the proline residues can be a terminal residue. Imino acids similar to proline, in that their side chains form a ring containing the peptide bonding nitrogen and α -carbon, and that will "break" an α -helix or β -sheet secondary structure, can be substituted for one or more of the proline residues. Exemplary peptides are shown as ~~SEQ. ID. Nos. 1-50~~ SEQ ID NOS: 1-50. The more preferred peptides are those of ~~SEQ. ID. NOS. 1-3, 11, 12, 29-33, 35-38, 40-41 and 44-50~~ SEQ ID NOS: 1-3, 11, 12, 29-33, 35-38, 40, 41, and 44-50.

Amend the paragraph starting in line 26 on page 8 as indicated:

Peptides Angio-2, Angio-3 and Angio-4, containing sequences from kringles 2, 3 and 4 of human plasminogen (~~SEQ. ID. Nos. 2, 3 and 11~~ SEQ ID NOS: 2, 3, and 11), all inhibited BAE cell proliferation in a dose-dependent manner (Figures 1, 2 and 3). The IC₅₀ of the three peptides are about 2 mM, 20 nM and 200 uM respectively. It is noted that peptide Angio-3 inhibited BAE cell proliferation with an IC₅₀ in a range similar to the reported nanomolar range of angiostatin protein (5). In contrast, a randomly scrambled version of Angio-3 (Angio-3S) in which the same amino acids present in Angio-3 were put in a random order, completely lost angiogenesis inhibition ability (Figure 1). This indicates that the antiangiogenic activity of the peptides are sequence dependent. No obvious cell cytotoxicity was observed by peptide angio-3 at 20μM with BAE cells analyzed by trypan blue staining and microscopic cellular morphology analysis.

Amend the paragraph starting in line 7 on page 9 as indicated:

The BAE inhibition assay provides a method for determining the anti-angiogenic activity of peptides. For example, peptides Angio-3A, -3B, -3C, -3D, -3E and -3F (~~SEQ. ID. Nos. 4-9~~ SEQ ID NOS: 4-9) are peptides in which the six amino acids surrounded by the two prolines are individually mutated into

alanine. The contribution of each of the six amino acids between the proline residues to the biological activity of Angio-3 can be determined by testing these peptides.